REMARKS

Applicant's attorney wishes to thank the Examiner for the careful consideration given to the present application. Currently, claims 1, 3, 5, 9-11 and 22 have been amended, claims 2, 4, 6-8, 12-21 and 23-24 have been canceled and new claims 25-26 have been added. Support for the new claims and amendments can be found in the specification as filed, for example, paragraphs [0086] and [0087] and thus, no new matter has been added. Applicant addresses each of the rejections set forth in the Office Action in the order presented therein.

Claim Objections

The Examiner has objected to claims 5 and 9 because they contain abbreviations. Applicant has amended claims 5 and 9 to conform to the Examiner's suggestions.

35 U.S.C. § 112

The Examiner has rejected claim 11 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant has amended claims 10 and 11 to recite a "peptide linker", thereby rendering this rejection moot.

35 U.S.C. § 103(a)

Claims 1-3, 5, 9, 10 and 22 are rejected under 35 U.S.C. § 103(a) as being obvious over Olsen (WO 00/64482) in view of either Yick or Zuo. Applicant respectfully disagrees.

Olsen discloses an "amphibody" comprised of at least two components, wherein the first component is capable of binding to a target and suppressing or inhibiting proteoglycans. Although Olson reflects an unmet need in the art, it neither discloses nor suggests the present chimeric chondroitinase compositions. Although Olson appreciates that it might be desirable to inhibit or suppress proteoglycans (e.g., page 22, lines 11 and 14) it does not suggest destroying proteoglycans. In fact, as acknowledged by Olson, proteoglycans are known to be "both positive and negative regulators of axonal growth" (see, e.g., page 25, lines 25-26). Accordingly,

viewing Olson as it would be seen in the art prior to the present invention, one ordinary skill in the art would not be motivated to destroy proteoglycans and cause harmful effects.

The remaining text on page 25 of Olson also supports this position, as it notes that after injury most, *but not all*, proteoglycans are upregulated and have inhibitory properties. Therefore, although Olson may be seen as encouraging the inhibition or suppression of proteoglycans, it is a misreading to say that it discloses or even suggests the use of an enzyme that results in the actual destruction of proteoglycans. Destruction of proteoglycans is achieved by using enzymes such as chondroitinases, hyaluronidases, and matrix metalloproteinases as set forth in the present claims.

In dealing with proteoglycans, none of the options mentioned by Olson include any enzymatic moiety. In contrast, Applicant's claimed invention is directed towards a chimeric protein comprising two polypeptides wherein a first polypeptide is an enzymatic moiety selected from the group consisting of chondroitinases, hyaluronidases, and matrix metalloproteinases. Chondroitinases, hyaluronidases, and matrix metalloproteinases are known enzymes that destroy proteoglycans. Olson actually teaches away from destruction of proteoglycans.

It would have not been obvious to one of ordinary skill in the art to link an enzymatic moiety to a chimer to achieve proteoglycan destruction and neurite growth. In particular, enzymes are complex and unpredictable compounds that exhibit variable functionalities under different steric conditions. Proper three-dimensional conformation, steric conformations and lack of steric hindrance are well-known in the art to be key aspects to the function of enzymes. There is also a concern that with chimers that contain enzymatic moieties there may be autocatalysis. Applicant is first to disclose a chimeric protein containing an enzymatic moiety that destroys proteoglycans.

Moreover, at the time of the present invention (and even after as noted below) proteoglycans were understood to have important roles in normal physiology. For example, Grumet et al Perspect Dev Neurobiol 1996; 3(4):319-330 (abstract) notes that differential expression of proteoglycans may be important for modulating cell adhesion as well as axonal

growth and guidance during development; notably, the continued expression of these molecules may prevent these processes from occurring unfettered in normal adult tissue.

Additionally, proteoglycans are known to be components of the perineuronal net. The perineuronal net could provide recognition molecules between certain neurons and their surrounding cells, and participate in the selection and consolidation of their relationship. (*See, e.g.*, Celio and Blumcke "perineuronal nets - a specialized form of extracellular matrix in the adult nervous system" Brain Res Brain Res Rev, 1994 Jan; 19(1):128-45) (abstract).

Even after the filing date, proteoglycans were understood to have important roles in the structure and healing of the adult nervous system. Rhodes and Fawcett J. Anat (2004) 204:33-48 at page 39 indicate that proteoglycans surrounding damaged tissue and disrupted blood brain barrier have a vital role is sealing off a lesioned area and that the proteoglycans may limit cavitation and secondary injury. Of note, it is suggested that if upregulation of proteoglycans were prevented that this might have "detrimental effects on the healing and sealing processes." Id.

Accordingly, degrading proteoglycans, prior to the findings of the present invention, would have been expected to have deleterious consequences, and would not be an obvious research choice. Again, neutralizing or suppressing proteoglycans of interest is far different than degrading and destroying them. Applicant was first to identify chimeric proteins for promoting repair and regeneration of neurons with the first component specifically capable of destroying proteoglycans. Yick, Zuo and Gearing fail to cure the deficiencies of Olsen. Therefore, for at least the reasons set forth above, Applicant submits that the pending claims are not obvious over Olsen in view of Yick, Zuo and Gearing. Accordingly, Applicant requests that the rejections associated with claims 1-3, 5, 9-11, and 22 be withdrawn.

In addition, Applicant has amended claim 22 to recite "a therapeutically effective amount" of a chimeric protein is used in a pharmaceutical composition with a pharmaceutically acceptable carrier. Applicant has added new claims 25-26 to refine the therapeutically effective amount. Olsen is silent to the cited therapeutically effective amount of a chimeric protein for promoting repair and regeneration of damaged neurons. Furthermore, Yick, Zuo and Gearing

fail to cure the deficiencies of Olsen. Therefore, for at least the reasons set forth above, Applicant submits that claim 22, as amended, and new claims 25 and 26 are not obvious in light of Olsen in view of Yick, Zuo and Gearing. Accordingly, Applicant requests that the rejections associated with claim 22 be withdrawn.

CONCLUSION

Applicant believes that the claims as presented are in condition for allowance, and notice to such effect is respectfully requested. Should the Examiner have any questions or comments, or need any additional information from Applicant's attorney, the Examiner is urged to contact the undersigned.

Applicant has timely filed this response. In the event that an additional fee is required for this response, the Commissioner is hereby authorized to charge such fees to Deposit Account No. 500436.

Respectfully submitted,
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Date: April 29, 2009